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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,409	03/12/2001	Timothy J. Kieffer	029996/0278721	1113

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EXAMINER	
PARAS JR, PETER	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 12/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,409	KIEFFER ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 June 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-70* is/are pending in the application.

4a) Of the above claim(s) *1-30 and 56-70* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6/20/03.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment received on 6/20/03 has been entered. Claims 38, 41, 42, 45, 46 and 54 have been amended. Claims 1-70 are pending. Claims 31-55 are under current consideration.

Applicant's amendment to the specification received on 9/26/03 has been entered.

Election/Restrictions

Claims 1-30 and 56-70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the amendment received on 9/18/02.

This application contains claims, 1-30 and 56-70, drawn to an invention nonelected without traverse in the amendment received on 9/18/02. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Sequence Compliance

The instant application is now in sequence compliance.

Information Disclosure Statement

Applicants have indicated that an IDS filed on 3/23/01 has not been considered by the Examiner. In response, the Examiner submits that there is no record of an IDS filed on 3/23/01 in the instant application. Applicants are encouraged to resubmit the IDS and corresponding references for consideration. The Examiner regrets any confusion resulting from the missing IDS.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 43-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The previous rejection is maintained for the reasons of record advanced on pages 3-5 of the Office action mailed on 12/18/02.

Applicants arguments filed on 6/20/03 have been fully considered but are not found persuasive. Applicants assert claims 43-44 are fully described by the instant specification. Applicants further assert that the sequences of the variants or subsequences need not be disclosed. Applicants point out that specification on page 13 discloses structural elements of the GIP promoter. In addition Applicants argue the

art is replete with examples of other gut promoters and enhancers such that a skilled artisan would be able to select variants and subsequences of such. See pages 4-8 of the amendment.

In response, the Examiner maintains that Applicants were not in possession of the variants and functional subsequences embraced by the claims. It is further maintained that the evidence of record fails to indicate that any of the claimed variants or subsequences of gut endocrine promoters even have the biological activity of a gut endocrine promoter. While Applicants specification has described various gut endocrine promoters, it is maintained the evidence of record has not described which variants or subsequences of gut endocrine promoters possess the biological activity of a gut endocrine promoter. The specification has disclosed that mutations in the distal and proximal GAT motifs reduced GIP promoter activity. However, the claim breadth embraces more than only GIP promoter variants comprising mutations in the proximal and distal GAT motifs. It is maintained that evidence of record has failed to provide a structural relationship between a gut endocrine promoter and any of the claimed variants or subsequences thereof. As such it is further maintained that one of skill in the art would not recognize that applicant was in possession of the necessary common features or attributes possessed by the functional variants or subsequences embraced by the claims.

Accordingly, the previous rejection is maintained for the reasons of record.

The written description rejection may be overcome if the claims are amended to only read on gut endocrine promoters.

Claims 31-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The previous rejection of claims 31-55 is maintained for the reasons of record advanced on pages 5-14 of the Office action mailed on 12/18/02.

Applicants arguments filed on 6/20/03 have been fully considered but are not found persuasive. Applicants argue the invention can be practiced without employing gene therapy, as the subject embraced by the claims is required to have transformed mucosal cells. Applicants assert the instant specification exemplifies an *in vivo* working model which does not employ gene therapy, as the subject animal is a transgenic mouse. Applicants further assert that Verma and Crystal only discuss general limitations of gene therapy. See pages 9-10 and 12 of the amendment.

In response, the Examiner maintains that the claims as written read on gene therapy. While the claims may be interpreted to read on a transgenic non-human animal the claims also read on gene therapy (*in vivo* and *ex vivo*), as the subject comprises cells transformed with a heterologous polynucleotide. If the claimed invention is intended to be directed to transgenic non-human animals then Applicant is encouraged to amend the claims to that end. In any event, Verma, Crystal, Anderson, Miller, and Deonarain set forth the unpredictability of the gene therapy art. See pages 7-9 of the Office action mailed on 12/18/02. It is maintained absent evidence to the

contrary that gene therapy is an unpredictable art. Accordingly, the rejection with respect to gene therapy is maintained.

Applicants submit that the Kieffer declaration provides data for another in vivo animal model in which a therapeutic protein (leptin) was produced in an amount sufficient to teat obesity. The Kieffer declaration relates to a mouse model for obesity, the ob/ob mouse. GTC-1pSwitch cells, which produce leptin when treated with RU486, were implanted into the ob/ob mouse and induced to produce leptin. The Kieffer declaration submits that the ob/ob mouse lost weight during RU486 administration as obesity was reduced by leptin secreted by implanted GTC-1 cells. See pages 10-11 of the amendment.

The Kieffer declaration under 37 CFR 1.132 filed 6/20/03 is insufficient to overcome the rejection of claims 31-55 based upon enablement as set forth in the last Office action because: The Kieffer declaration while providing a working example relating to *ex vivo* gene therapy fails to enable the full scope of the claimed methods. The claims are overly broad as they relate to any disease and any therapeutic protein. While the Kieffer declaration provides evidence of treatment of obesity using the ob/ob mouse comprising implanted GC-1pSwitch cells the Kieffer declaration fails to provide evidence of treatment of other diseases embraced by the claims.

Applicants argue the instant specification indicates that non-β cells can be used for insulin production, that such cells secrete insulin in response to glucose, and that the insulin produced is properly processed. Applicants submit that such evidence is adequate to refute Yoon et al.

In response, the Examiner maintains the instant claims read on gene therapy. The specification has discussed production of human insulin by K cells in a transgenic mouse. However, the claims do not appear limited to a transgenic mouse producing human insulin. It is maintained that *in vivo* gene delivery to the gut (K cells) need to be developed for successful treatment of IDDM. See Yoon and Corbett on pages 10-12 of the Office action mailed on 12/18/02.

The aspect of the rejection directed to treatment of obesity is maintained. See pages 12-13 of the Office action mailed on 12/18/02 as well as Buettner et al.

Accordingly, the rejection is maintained for the reasons of record.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time). The examiner is scheduled to move a new office, on 1/13/2004, having a new telephone number as follows: 571-272-0732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER